PB86-213220

Effects of Microwave Radiation on the Blood-Brain Barrier

(U.S.) Health Effects Research Lab.
Research Triangle Park, NC

May 86

U.S. Department of Commerce
National Technical Information Service
NTIS

PB86-213220

EPA/600/D-86/113
May 1986

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TECHNICAL REPORT DATA (Please read Instructions on the reverse before completing)		
1. REPORT NO. EPA/600/D-86/113	2.	3. RECIPIENT'S ACCESSION NO. PB86-213220/AS
4. TITLE AND SUBTITLE EFFECTS OF MICROWAVE RADIATION ON THE BLOOD-BRAIN BARRIER		5. REPORT DATE May 1986 6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S) Thomas Ward, Joseph S. Ali and Merritt D. Long		8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS Health Effects Research Laboratory Office of Research and Development U. S. Environmental Protection Agency Research Triangle Park, NC 27711		10. PROGRAM ELEMENT NO. 11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Health Effects Research Laboratory Office of Research and Development U. S. Environmental Protection Agency Research Triangle Park, NC 27711		13. TYPE OF REPORT AND PERIOD COVERED 14. SPONSORING AGENCY CODE EPA/600/11
15. SUPPLEMENTARY NOTES		

16. ABSTRACT

We attempted to repeat a portion of the study by Oscar and Hawkins in which pulsed and continuous wave microwave radiation increased permeation of labeled tracers through the blood-brain barrier. At the SAR used (0.1 W/kg) the calculated average brain temperature rise is less than 0.1 °C. We found no changes in permeation, however, there were differences in experimental conditions, including type of tracers, frequency and microwave field configuration. It is possible but unlikely that one of these differences is responsible for the apparent discrepancy in results.

17. KEY WORDS AND DOCUMENT ANALYSIS		
a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
18. DISTRIBUTION STATEMENT RELEASE TO PUBLIC	19. SECURITY CLASS (This Report) UNCLASSIFIED 20. SECURITY CLASS (This page) UNCLASSIFIED	21. NO. OF PAGES 10 22. PRICE $9.95

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

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Effects of Microwave Radiation on the Blood-Brain Barrier

In 1977 Oscar and Hawkins published the results of a study in which microwave radiation increased permeation of several radio-labeled compounds through the blood-brain barrier of rats. In 1978 Merritt et al. attempted to but could not replicate this work. The interpretation of the results of this latter publication is controversial (Justesen 1980).

In this study we attempted to repeat the exposure conditions in the Oscar and Hawkins' study where the increase was most pronounced. Figure 4 (p. 288, Oscar and Hawkins) shows increased permeation of mannitol at both continuous wave (CW) and pulsed (1000 pps, 0.5 μs pulse width) radiation at an average power density of 0.3 to 0.5 mW/cm^2 [SAR ≈ 0.1 mW/g (Durney, 1978)]. We used CW and the same pulse parameters but contraints on equipment necessitated some important differences in experimental conditions. Where they used 1.3 GHz whole animal exposures in the far field, we exposed the head only in a waveguide at 1.7 GHz (the average SAR of the head was 0.1 W/kg). Other changes which made our assay more sensitive to changes in permeation than the earlier study included measurement of permeation during exposure and calculation of transfer constants (Blasburg, 1979) instead of the brain uptake index (Oldendorf, 1970).

Materials and Methods

The procedures used in the measurement of brain uptake of radio-labeled tracers were similar to those described earlier (Ward et al. 1982), where the labeled tracer compounds were injected intravenously into rats prior to exposure. Then, after a 30 min exposure the brain is perfused, sectioned, and the sections assayed for uptake of the tracer compounds. The waveguide exposure system was powered by an AIL 125 generator which had been modified to accept a high voltage

supply and a pulse generator for the pulsed exposures. The pulse parameters were continuously monitored with an oscilloscope. The rat's head was positioned through a 3.8 cm (1.5 inch) hole in the waveguide. The animal and waveguide were located in a chamber in which the temperature was controlled at 28 ± 0.5 °C. Absorbed power was determined by substracting the reflected and transmitted power from the incident power. Transfer constants (Ki) were calculated by:

$$Ki = C_b / \int_0^{40} C_s dt \qquad \text{Equation 1}$$

where C_b and C_s are the brain and serum tracer concentrations respectively. The integral in the above expression represents the brain's total exposure to the tracers. The value of the integral was estimated from blood samples taken at 2 and 40 min (Ward et al. 1982).

Brain temperatures were measured during exposure by inserting a non-perturbing temperature probe (Vitex, model 101) into different brain regions of anesthesized rats. Average increases in temperature can be calculated by:

$$\Delta T = t \cdot SAR/K \cdot C \qquad \text{Equation 2}$$

where ΔT is change in temperature in °C, t is time in seconds, SAR is specific absorption rate in W/kg, K is 4.2 joules/cal, and C is the specific heat capacity of brain (880 cal/°C per kg).

Results and Discussion

Regional brain and body core temperatures are shown in Table 1. Although some variability in the data is evident, the average increase for all brain regions is 0.2 °C for the exposed animals. This compares to a value of 0.05 °C calculated using the SAR of 0.1 W/kg in Equation 2. The data presented for brain regions are individual measurements and not means. Also note these exposures were at 2.45 GHz and not at 1.7 GHz. This difference in frequency could result in different areas of high energy deposition and perhaps in different heating patterns. Yet the thermal gradients within the brain would be minimal. The

average heating rate of 2.7×10^{-5} °C/s (for an SAR of 0.1 W/kg) can be calculated by dividing each side of Equation 2 by time. With blood flow and conduction dispersing the heat, temperature gradients within the brain should be small.

The transfer constants (Ki) for inulin and sucrose are shown in Tables 2 and 3. When analyzed by one way analysis of variance, no significant change in permeation was found for any region with either tracer at pulsed or CW irradiation. The values for regions were averaged to find a whole brain average, but no change in the permeation was found as a result of the microwave exposures.

Conclusion

We attempted to repeat a portion of the study by Oscar and Hawkins in which pulsed and continuous wave microwave radiation increased permeation of labeled tracers through the blood-brain barrier. At the SAR used (0.1 W/kg) the calculated average brain temperature rise is less than 0.1 °C. We found no changes in permeation, however, there were differences in experimental conditions, including type of tracers, frequency and microwave field configuration. It is possible but unlikely that one of these differences is responsible for the apparent discrepancy in results.

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Table 1

Brain and Body Core Temperatures (°C)

Brain Region	Sham			0.1 W/kg		
	Initial	Final	ΔT	Initial	Final	ΔT
Cortex	36.4	36.2	-0.2	36.8	37.0	+0.2
Cerebellum	36.4	36.8	+0.4	36.1	36.3	+0.2
Medulla	37.1	37.0	-0.1	37.5	37.1	-0.4
Striatum	35.4	35.6	+0.2	35.8	35.8	0
Hypothalamus	36.7	36.7	0.0	37.1	37.5	+0.4
Hippocampus	36.2	36.3	+0.1	35.3	35.7	+0.4
Midbrain	36.3	36.4	+0.1	36.3	36.6	+0.3
Olfactory Lobes	35.4	35.1	-0.3	35.5	35.7	+0.2
Body Core	36.1	36.1	0.0	36.0	36.1	+0.1

- Each regional brain temperature was measured in a separate animal
- These are individual measurements and not means except for body core temperature
- Exposures were at 2.45 GHz CW

Table 2

Brain Uptake of Inulin

Region	Transfer Constants ($x10^4$, min^{-1})			P[a]
	Sham mean ± SEM	CW mean ± SEM	Pulsed mean ± SEM	
Cortex (Front)	1.87 ± .09	2.02 ± .09	1.70 ± .15	.14
Cortex (Lateral)	1.73 ± .09	1.97 ± .14	1.62 ± .15	.16
Cerebellum	1.83 ± .10	1.93 ± .13	1.70 ± .13	.38
Medulla	1.59 ± .08	1.65 ± .10	1.51 ± .10	.57
Striatum	1.39 ± .12	1.49 ± .12	1.39 ± .16	.85
Hypothalamus	1.74 ± .11	1.76 ± .10	1.55 ± .13	.34
Hippocampus	1.47 ± .09	1.66 ± .13	1.43 ± .13	.39
Midbrain	1.53 ± .08	1.54 ± .08	1.37 ± .12	.37
Olfactory Lobes	1.91 ± .14	2.05 ± .13	2.04 ± .21	.80
Average brain	1.67 ± .09	1.79 ± .09	1.59 ± .13	.43

[a] Analyzed by one way analysis of variance
n = 9 for each treatment group

Table 3

Brain Uptake of Sucrose

Region	Transfer Constants (x 10^4, min^{-1})			P[a]
	Sham mean ± SEM	CW mean ± SEM	Pulsed mean ± SEM	
Cortex (Front)	2.99 ± .17	2.99 ± .11	2.92 ± .10	.89
Cortex (Lateral)	2.78 ± .16	2.89 ± .12	2.78 ± .09	.79
Cerebellum	2.95 ± .17	3.04 ± .13	3.00 ± .13	.91
Medulla	2.57 ± .14	2.70 ± .10	2.65 ± .08	.74
Striatum	2.29 ± .19	2.26 ± .11	2.36 ± .11	.86
Hypothalamus	2.83 ± .20	2.78 ± .11	2.81 ± .10	.98
Hippocampus	2.24 ± .15	2.23 ± .09	2.32 ± .11	.84
Midbrain	2.69 ± .14	2.66 ± .12	2.73 ± .09	.89
Olfactory Lobes	3.48 ± .21	3.43 ± .16	3.53 ± .14	.91
Average brain	2.76 ± .16	2.78 ± .09	2.79 ± .10	.98

[a] Analyzed by one way analysis of variance
n = 9 for each treatment group